CURRICULUM VITAE

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EDUCATION

Jan. 1992 – Oct. 1994 **M.Sc.** (Biochemistry & Molecular Biology); The University of British Columbia, Vancouver, Canada.

Sept. 1987 – Apr. 1991 **B.Sc. (Hon)** (Biochemistry); The University of British Columbia, Vancouver, Canada.

RESEARCH EXPERIENCE

Jan. 2003 – present **Research Scientist IV**, Inex Pharmaceuticals Corp., Vancouver, Canada.
Project: Evaluation and pre-development of Inex's conventional drug pipeline candidates.

Jan. 2001 – Dec. 2002 **Research Scientist III**, Inex Pharmaceuticals Corp., Vancouver, Canada.
Project: Project leader; development and evaluation of lipid-based delivery systems for vaccines and tumor immunotherapy.

- Managed and performed efficacy and immunology studies to characterize a liposomal oligonucleotide formulation for vaccine delivery
- Managed multiple research collaborations and CROs

June 1999 – Jan. 2001 **Research Scientist II**, Inex Pharmaceuticals Corp.
Project: Project leader; development and evaluation of lipid-based delivery systems for antisense oligonucleotides, conventional anticancer drugs, and immune stimulation.

- Managed antisense research collaborations with Regina Elena Cancer Institute, Peter MacCallum Cancer Institute, G. Gaslini Children's Hospital (Laboratory of Oncology), University of Alberta (T. Allen)
- Coordinated and generated liposomal topotecan pre-clinical efficacy package for successful partnering with GSK

Apr. 1996 – June 1999 **Research Scientist I**, Inex Pharmaceuticals Corp.
Project: Project leader; development and evaluation of lipid-based delivery systems for antisense oligonucleotides and ribozymes.

EXHIBIT
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- Managed antisense and ribozyme research collaborations with Isis Pharmaceuticals, Ribozyme Pharmaceuticals, Gilead/Glaxo, Regina Elena Cancer Institute, INSERM-Marseille; coordinated PK/ADME and NHP study with Sierra Biomedical for INXC-6295.
- Coordinated and performed pre-clinical efficacy and toxicology studies for INXC-6295 IND, prepared study reports and summaries for successful IND application.

Sept. 1995 – Apr. 1996 **Research Associate II**, Inex Pharmaceuticals Corp.
Project: Evaluation of lipid-based formulations of ICAM-1 antisense oligonucleotides as anti-inflammatory agents.

Oct. 1994 – Aug. 1995 **Research Associate I**, Inex Pharmaceuticals Corp.
Project: Development of inflammation models for evaluating the activity of ICAM-1 antisense oligonucleotides.

Jan. 1992 – Oct. 1994 **Graduate Student**, Supervisor: Dr. P.R. Cullis, Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, Canada.
Project: The influence of lipid composition on the interaction of liposomes with plasma proteins.

May 1991 – Sept. 1991 **MRC Summer Studentship**, Supervisor: Dr. D.V. Devine, Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada.
Project: Factors influencing the activation of rat complement by liposomes

Sept. 1990 – Apr. 1991 **Honours Thesis (B.Sc.)**, Supervisor: Dr. P.R. Cullis, Department of Biochemistry, University of British Columbia, Vancouver, Canada.
Project: Identification of plasma proteins that interact with liposomes *in vivo*.

May 1990 – Aug. 1990 **Summer Studentship**, Supervisor: Dr. P.R. Cullis, Department of Biochemistry, University of British Columbia, Vancouver, Canada.
Project: Development of methods for isolating plasma proteins from liposomes

AWARDS

University of British Columbia Entrance Scholarship, 1987

Medical Research Council of Canada Summer Studentship, 1991

Evelyn Hartman Memorial Scholarship (leadership, scholastic achievement), 1993

PUBLICATIONS

1. Stuart, D.D., **Semple, S.C.** and Allen, T.M. High efficiency entrapment of antisense oligonucleotides in liposomes. *Methods Enzymol.*, in press, 2003.

2. Pastorino, F., Brignole, C., Marimpietri, D., Pagnan, G., Morando, A., Ribatti, D., Semple, S.C., Gambini, C., Allen, T.M., Ponzoni, M. Targeted Liposomal C-myc Antisense Oligodeoxynucleotides Induce Apoptosis and Inhibit Tumor Growth and Metastases in Human Melanoma Models. *Clin. Cancer Res.*, in press, 2003

3. Mui, B., Raney, S.G., **Semple, S.C.** and Hope, M.J. Immune stimulation by a CpG-containing oligodeoxynucleotide is enhanced when encapsulated and delivered in lipid particles. *J. Pharmacol. Exp. Ther.* 298(3), 1185-1192, 2001.

4. Maurer, N., Wong, K.F., Stark, H., Louie, L., McIntosh, D., Wong, T., Scherrer, P., **Semple, S.C.**, Cullis, P.R. Spontaneous entrapment of polynucleotides upon electrostatic interaction with ethanol-destabilized cationic liposomes. *Biophys. J.* 80(5), 2310-2326, 2001.

5. Leonetti, C., Biroccio, A., Benassi, B., Stringaro, A., Stoppacciaro, A., **Semple, S.C.**, Zupi, G. Encapsulation of c-myc antisense oligodeoxynucleotides in lipid particles improves antitumoral efficacy in vivo in a human melanoma line. *Cancer Gene Ther.* 8(6), 459-468, 2001.

6. **Semple, S.C.**, Klimuk, S.K., Harasym, T.O., Dos Santos, N., Ansell, S.M., Wong, K.F., Maurer, N., Stark, H., Cullis, P.R., Hope, M.J. and Scherrer, P. Efficient encapsulation of antisense oligonucleotides in lipid vesicles using ionizable aminolipids: formation of novel small multilamellar vesicle structures. *Biochim. Biophys. Acta.* 1510, 152-166, 2001.

7. Bramson, J.L., Bodner, C.A., Kojic, L.D., **Semple, S.**, Johnson, J., and Hope, M.J. Intravenous administration of stabilized antisense lipid particles (SALP) leads to activation and expansion of liver NK cells. *Antisense Nucleic Acid Drug Dev.* 10, 217-224, 2000.

8. Klimuk, S.K., **Semple, S.C.**, Nahirney, P.N., Mullen, M.C., Bennett, C.F., Scherrer, P and Hope, M.J. Enhanced anti-inflammatory activity of a liposomal intercellular adhesion molecule-1 antisense oligodeoxynucleotide in an acute model of contact hypersensitivity. *J. Pharmacol. Exp. Ther.* 292(2), 480-488, 2000.

9. **Semple, S.C.**, Klimuk, S.K., Harasym, T.O. and Hope, M.J. Lipid-based formulations of antisense oligonucleotides for systemic delivery applications. *Methods Enzymol.* 313, 322-341, 2000.

10. Webb, M.S., Klimuk, S.K., **Semple, S.C.** and Hope, M.J. Lipid-based carriers for the systemic delivery of antisense drugs. In *Manual of Antisense Methodology.* Hartmann, G. and Endres, S., Eds. Kluwer Academic Publishers, pp. 167-190, 1999.

11. Ansell, S.M., Kojic L.D., Hankins, J.S., Sekirov, L., Boey, A., Lee, D.K., Bennett, A.R., Klimuk, S.K., Harasym, T.O., Dos Santos, N. and **Semple, S.C.** Application of octa-(14-amino-3,6,9,12-tetraoxatetradecanoic acid) lipid conjugates as steric barrier molecules in liposomal formulations. *Bioconjug. Chem.* 10, 653-666, 1999.

12. Klimuk, S.K., **Semple, S.C.**, Scherrer, P. and Hope, M.J. Contact hypersensitivity: a simple model for the characterization of disease-site targeting by liposomes. *Biochim. Biophys. Acta* 1417, 191-201, 1999.

13. **Semple, S.C.**, Chonn, A. and Cullis, P.R. Interactions of liposomes and lipid-based carrier systems with blood proteins: relation to clearance behaviour in vivo. *Adv. Drug Del. Rev.* 32 (1/2), 3-17, 1998.

14. **Semple, S.C.** and Chonn, A. Liposome-blood protein interactions in relation to liposome clearance. *J Liposome Res.* 6(1), 33-60, 1996.

15. Oja, C.D., **Semple, S.C.**, Chonn, A. and Cullis, P.R. Influence of dose on liposome clearance: critical role of blood proteins. *Biochim. Biophys. Acta* 1281, 31-37, 1996.

16. **Semple, S.C.**, Chonn, A. and Cullis, P.R. Influence of cholesterol on the association of plasma proteins with liposomes. *Biochemistry* 35, 2521-2525, 1996.

17. Chonn, A., **Semple, S.C.** and Cullis, P.R. β2-glycoprotein I associates with very rapidly cleared liposomes in vivo suggesting a major role in the immune clearance of "non-self" particles. *J. Biol. Chem.* 270, 25845-25849, 1995.

18. Chonn, A., **Semple, S.C.** and Cullis, P.R. Protein-membrane interactions in the biological milieu. In *Biological Membranes: Structure, Biogenesis and Dynamics.* J.A.F. Op den Kamp, Ed. Springer-Verlag Publishers. 82, pp. 101-106, 1994.

19. Chonn, A., **Semple, S.C.** and Cullis, P.R. Association of blood proteins with large unilamellar liposomes in vivo: relation to circulation lifetimes. *J Biol. Chem.* 267, 18759-18765, 1992.

20. Chonn, A., **Semple, S.C.** and Cullis, P.R. Separation of large unilamellar liposomes from blood components by a spin column procedure: towards identifying plasma proteins which mediate liposome clearance in vivo. *Biochim. Biophys. Acta* 1070, 215-222, 1991.

MANUSCRIPTS (submitted or in preparation)

21. **Semple, S.C.**, Harasym, T.O., Clow, K., Kojic, L., Ansell, S.M., Klimuk, S.K. and Hope, M.J. Immunogenicity and rapid plasma elimination of non-viral delivery systems for gene and antisense therapy. *Proc. Natl. Acad. Sci. USA*, submitted.

22. **Semple, S.C.**, Bramson, J.L., Ludkovski, O., Clow, K., Klimuk, S.K., Hope, M.J. and Harasym, T.O. Enhanced potency of phosphorothioate c-myc antisense oligodeoxynucleotides in murine and human tumor models upon systemic administration of stabilized antisense-lipid particles. *Antisense Nucl. Acid Drug Des.*, submitted.

23. Sandberg, J.A., Min, J.J., Jensen, K.L., Bouhana, K.S., Gallegos, A.M., Klimuk, S.K., **Semple, S.C.**, Scherrer, P., Hope, M.J., Parry, T.J. and Reynolds, M.A. Lipid-based carriers enhance the biodistribution and efficacy of anti-angiogenic ribozyme in a murine Lewis lung carcinoma model. *Proc. Natl. Acad. Sci. USA*, submitted.

24. **Semple, S.C.**, Ahkong, L., Leng, E., Mui, B., Hope, M.J. and Klimuk, S.K. Pre-clinical anti-tumor activity of liposomal topotecan: increased efficacy and therapeutic index of liposomal topotecan in murine and human xenograft tumor models compared to free drug. *Clin. Cancer Res.*, in preparation.

25. **Semple, S.C.**, Klimuk, S.K., Clow, K., Dos Santos, N., Hope, M.J, Nation, N., Kornbrust, D.and Harasym, T.O. Toxicity of lipid-based formulations of phosphorothioate c-myc antisense oligodeoxynucleotides in rodents and non-human primates. *J. Pharmacol. Exp. Ther.*, in preparation.

PUBLISHED ABSTRACTS

1. **Semple, S.C.**, Mui, B., Hope, M.J., Madden, T.J., Leone, R., Ahkong, Q.-F., Cullis, P.R., McCabe, F.L., Johnson, R.K., Henry, M., Klimuk, S.K. Comparative efficacy and therapeutic index of topotecan and liposomal topotecan in murine and human solid tumor models. *Proc. Amer. Assoc. Cancer Res.* 44(2), 728-729, 2003.

2. Klimuk, S.K., Yuan, Z.-N., Leng, E., Leone, R., Lam, K., Ahkong, Q.-F., Cullis, P.R., **Semple, S.C.** Anti-tumor activity and therapeutic index of liposomal vinorelbine in human solid tumor xenografts. *Proc. Amer. Assoc. Cancer Res.* 44(2), 729, 2003.

3. Leonetti, C., Scarsella, M., D'Angelo, C., **Semple, S.C.**, Zupi, G. Liposome-encapsulated vincristine exhibits significant anti-tumor activity against vincristine-resistant human solid tumors. *Proc. Amer. Assoc. Cancer Res.* 44(2), 747, 2003.

4. Brignole, C., Pastorino, F., Marimpietri, D., Pagnan, G., Ribatti, D., **Semple, S.**, Gambini, C., Allen, T., Ponzoni, M. Anti-GD2 targeted liposomal c-myc antisense oligodeoxynucleotides inhibit metastases and tumor growth in human melanoma tumor models. *Proc. Amer. Assoc. Cancer Res.* 44(2), 1289, 2003.

5. Yuan, Z.-N., Klimuk, S.K. and **Semple, S.C.** Mucosal immune responses induced by immunostimulatory oligonucleotides are enhanced when formulated in lipid particles. *FASEB J.* 16(4), A680, 2002.

6. Klimuk, S.K., Yuan, Z.-N., Ansell, S.M., **Semple, S.C.** Characterization of a liposomal cancer vaccine delivery system containing immunostimulatory oligonucleotides. *Proc. Amer. Assoc. Cancer Res.* 43, 447, 2002

7. **Semple, S.C.**, Klimuk, S.K., MacLachlan, I., Leng, E., Mui, B. and Hope, M.J. Pre-clinical evaluation of liposomal topotecan: increased efficacy and therapeutic index in murine and human xenograft tumor models compared to free drug. *Proc. Amer. Assoc. Cancer Res.* 42, 374, 2001.

8. **Semple, S.C.**, Klimuk, S.K., Mui, B. and Hope, M.J. Encapsulation of immunostimulatory oligonucleotides in lipid particles dramatically increases immune responses and leads to effective tumor immunotherapy in mice. *Proc. Amer. Assoc. Cancer Res.* 42, 820-821, 2001

9. **Semple, S.C.**, Bramson, J.L, Ludkovski, O., Clow, K., Dos Santos, N., Joshi, P. Klimuk, S.K., Hope, M.J. and Harasym, T.O. Pre-clinical studies with stabilized antisense-lipid particles (SALP) containing c-myc antisense oligonucleotides. *J. Liposome Res.* 10(2/3), 277-278, 2000.

10. **Semple, S.C.**, Clow, K., Harasym, T.O., Airriess, R.A., Klimuk, S.K. and Hope, M.J. Immunogenicity and rapid blood elimination of PEG-liposomes containing entrapped nucleic acid upon repeat administration. *J. Liposome Res.* 10(2/3), 278, 2000.

11. Ahkong, L., Airriess, R., Harasym, T., Hope, M., Klimuk, S., Leng, E., MacLachlan, I., **Semple, S.C.**, Tam, P. and Hope, M.J. Pre-clinical studies with liposomal mitoxantrone: formulation, pharmacokinetics, toxicity and efficacy. *J. Liposome Res.* 10(2/3), 199-200, 2000.

12. Mui, B., Raney. S., **Semple, S.C.**, and Hope, M.J. Encapsulation enhances the induction of cytokines by oligodeoxynucleotides containing an immunostimulatory CpG motif. *J. Liposome Res.* 10(2/3), 229-230, 2000.

13. Maurer, N., Wong, K.F., Louie, L., McIntosh, D., Stark, H., **Semple, S.C.**, Wong, T., Scherrer, P. and Cullis, P. Spontaneous entrapment of polyelectrolytes upon electrostatic interaction with ethanol-destabilized liposomes. *J. Liposome Res.* 10(2/3), 254-255, 2000.

14. Leonetti, C., Biroccio, A., Benassi, B., **Semple, S.C.**, and Zupi, G. Encapsulation of c-myc antisense oligodeoxynucleotides in stabilized antisense-lipid particles improves antitumoral efficacy in human melanoma xenografts. *Proc. Amer. Assoc. Cancer Res.* 41, 642, 2000.

15. **Semple, S.C.**, Klimuk, S.K., Harasym, T.O, Scherrer, P., Dos Santos, N., Ansell, S.M., Lutwyche, P. and Hope, M.J. Stabilized antisense-lipid particles (SALP) for systemic applications: generation, characterization and in vivo properties. *J. Liposome Res.* 8(1), 104-105, 1998.

ABSTRACTS

1. **Semple, S.C.**, Bramson, J.L., Raney, S.G., Klimuk, S.K., Hope, M.J. and Mui, B. "Stabilized antisense-lipid particles (SALP) strongly enhance the immune stimulation of CpG

oligodeoxynucleotides: an 'artificial virus' approach to cancer vaccines." Cancer Vaccines 2000, New York, USA (October, 2000).

2. **Semple, S.C.**, Klimuk, S.K., C. Frank Bennett, Michael J. Hope and Scherrer, P. "Lipid-based delivery systems enhance the biological properties of antisense oligonucleotides." Gordon Research Conference on Drug Carriers in Biology and Medicine, Ventura, California, USA (February, 1998).

3. **Semple, S.C.**, Klimuk, S.K., Scherrer, P, C. Frank Bennett and Michael J. Hope. "Transmembrane carrier systems (TCS) enhance the biological properties of antisense oligonucleotides." 4th Cambridge Symposium: Oligonucleotide Chemistry and Biology, Cambridge, England (August, 1997).

4. Reynolds, M.A., Min, J., Jensen, K., Bouhana, K., Parry, T., Sandberg, J.A., **Semple, S.C.**, Klimuk, S.K. and Scherrer, P. "Long-circulating liposome formulations of chemically stabilized hammerhead ribozymes: biodistribution studies in a murine metastatic tumor model." 4th Cambridge Symposium: Oligonucleotide Chemistry and Biology, Cambridge, England (August, 1997).

5. **Semple, S.C.**, Klimuk, S.K., Scherrer, P. and Hope, M.J. "Liposome encapsulation of antisense oligonucleotides decreases complement activation." International Congress: Therapeutic Oligonucleotides, Rome, Italy (June, 1996).

6. Klimuk, S.K., **Semple, S.C.**, Scherrer, P. and Hope, M.J. "Increased circulation lifetime and accumulation of liposomal antisense at a site of inflammation." International Congress: Therapeutic Oligonucleotides, Rome, Italy (June, 1996).

7. Klimuk, S.K., **Semple, S.C.**, Scherrer, P. and Hope, M.J. "Enhanced anti-inflammatory activity of liposomal ICAM-1 antisense oligonucleotides." International Congress: Therapeutic Oligonucleotides, Rome, Italy (June, 1996).

8. **Semple, S.C.**, Chonn, A., and Cullis P.R. "Liposome-blood protein interactions in relation to clearance phenomena." Liposomes: The Next Generation, Liposome Research Days Conference, Vancouver, Canada (June, 1994).

9. Oja, C.D., **Semple, S.C.**, Chonn, A., and Cullis P.R. "Effect of dose on liposome clearance: RES saturation revisited." Liposomes: The Next Generation, Liposome Research Days Conference, Vancouver, Canada (June, 1994).

10. **Semple, S.C.**, Chonn, A., and Cullis P.R. "Interactions of plasma proteins and saturated phosphatidylcholine liposomes: the influence of cholesterol." Western Canada Biomembranes Conference, Whistler, Canada (December, 1992).

INVITED PRESENTATIONS

1. *"In Vivo* Properties of a Liposomal Delivery System for Antisense and Immunostimulatory Oligonucleotides", Gene Delivery: Non-Viral Systems and In Vivo Applications, San Diego, CA (December, 2002)

2. "Immunological properties of liposome-encapsulated oligonucleotides", 8th Liposome Research Days, Berlin, Germany (May, 2002)

3. "Stabilized antisense-lipid particles: applications for the delivery of antisense and immunostimulatory oligonucleotides. Gene Delivery Systems: Improving Pathways, Efficiency and Stability, Washington, DC (December, 2001)

4. "Preclinical studies with stabilized antisense-lipid particles (SALP) containing c-myc antisense oligonucleotides", 7th Liposome Research Days Conference, Napa Valley, CA (April, 2000).

5. "Preclinical studies with SALP (Stabilized Antisense-Lipid Particles) employing novel lipids", 6th Annual Sierra Biomedical Symposium, San Diego, CA (May, 1999).